Attorney Docket No. 9701-6 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Cumming et al. Group Art Unit: 1639
Serial No.: 09/510.560 Examiner: J. Lundgren
Filed: February 22, 2000 Confirmation No. 3011
For: *Solid Oral Dosage Form Containing an Enhancer*

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Declaration of Thomas W. Leonard, Ph.D.
Pursuant to 37 C.F.R. § 1.132

I, Thomas W. Leonard, do hereby declare and say as follows:

1. I have a Ph.D. degree in pharmaceutics from the Medical College of Virginia in Richmond, VA. I am Vice President and Chief Scientific Officer of Merrion Pharmaceuticals, LLC in Wilmington, NC, the assignee of the present application. I have been conducting research in the area of pharmaceutical formulations for more than 25 years and have authored or co-authored more than 30 publications related to this area. I have also been named as inventor or co-inventor on 39 patents and patent applications related to pharmaceutical formulations. A copy of my curriculum vitae is attached as Exhibit A.

2. I have read and understood the Official Action mailed September 17, 2008 (the "Action"), including the rejection of all pending claims for obviousness. The claims are directed to solid oral dosage forms which are effective in delivering a drug and an enhancer to an intestine, consisting of a hydrophilic or macromolecular drug, one or more absorption enhancers each of which is a salt of a medium chain fatty acid having a carbon length of from 8 to 14 carbon atoms and is a solid at room temperature, and one or more listed excipients.

3. The following experiments have been carried out under my instruction and supervision to demonstrate the differences between using medium chain fatty acids and medium chain fatty acid salts as enhancer systems in tablets, conventional capsules, and dry powders intended to deliver orally poorly absorbed hydrophilic active substances.

A. Powder Flow Evaluation

4. In order to make tablets and conventional capsules in an automated fashion, suitable for making more than a handful of units, the powder or granulation to be compressed

must flow from the machine hopper into the tablet die or capsule shell body prior to the application of pressure to make the tablet or placement of the capsule shell top respectively. Merrion currently has ongoing clinical trials using tablets made with medium chain fatty acid salts that have been made in an automated fashion using standard pharmaceutical processing equipment. These tablets meet all necessary commercial attributes (i.e., acceptable content uniformity, physical and chemical stability, appearance, etc.), and are appropriate commercial material. Several thousand tablets have been produced of several different products and strengths. Medium chain fatty acid salts alone can be used to make a tablet or capsule without the aid of any tableting excipients. Simple mixtures of medium chain fatty acid salts and pharmaceutical excipients such as a sugar (lactose, mannitol, or sorbitol) can also be used to make tablets or capsules. The latter procedure is used to make tablets that are being studied in the clinic. A ratio of 5 to 1 for fatty acid to excipient has been used very successfully to make tablets.

5. Determining the flow characteristics of powders using a flow meter and calculating the angle of repose is a valuable way to evaluate the ability of the powder to flow smoothly and reproducibly into a die, thereby enabling creation of tablets or capsules. Flow evaluation was carried out on the following four powders to evaluate their ability to make tablets and capsules and this value was used to calculate an angle of repose (**Table 1**). In general, materials with an angle of repose of less than 40° are considered acceptable for commercial production. Values less than 35° are considered good flow (Monograph 2.9.36. Powder flow, *European Pharmacopoeia 6.0*). The flows for sodium caprate and the sodium caprate/sugar combination indicate that they are very suitable materials for pharmaceutical processing. The total lack of flow of the capric acid and the capric acid/sugar combination, even with a 25 mm aperture, precludes the calculation of an angle of repose and indicates that these materials cannot be used to manufacture tablets or capsules.

Table 1. Flow evaluation carried out on 4 different powders.

Material	Flow	Angle of repose
Sodium Caprate	233.0sec/100g (10mm aperture)	35.2°
Sodium Caprate/Sorbitol 5/1	152.7sec/100g (10mm aperture)	32.1°
Capric acid	Does not flow (25mm aperture)	NA
Capric Acid/sorbitol 5/1	Does not flow (25mm aperture)	NA

6. Based on visual observation from this experiment, it appears that the particle size of the capric acid might be impeding the materials' ability to flow. Accordingly, the capric acid powder and the capric acid /sorbitol powder were each passed manually through a 1 mm screen to reduce particle size. This is a very low shear method to reduce particle size, and represents a fraction of the energy input that commercial techniques require. The capric acid and the capric acid/sorbitol mixture were both very difficult to screen manually due to capric acid's very low melting point. Passage of the material through the screen was sufficient to cause melting to occur. Only small amounts of material passed through the screen before the screen became blocked with melted capric acid. This was true with both powders. The use of a high melting point material such as sorbitol can act to coat the particles of the low melting material, and thus

facilitate the milling of the material using the screen. However, the melting point of the capric acid is too low for this technique to be of benefit. These screened materials did not flow, and, in fact, had less potential to flow than the original powders. **Figure 1** is a picture of the screen after an attempt was made to pass the capric acid/sorbitol powder through it. It can be noted that the screen is clogged with melted capric acid. No picture is shown of a screen after sodium caprate was passed through it, as it bears no difference in appearance from an unused and clean screen. Please note that no supplemental particle reduction was necessary to create tablets using sodium caprate; this activity was carried out to show the substantial differences in the materials.

B. Tableting Evaluation

7. Attempts were made to prepare tablets using 550 mg of capric acid and sodium caprate alone. These two materials were blended with 20% w/w sorbitol, and the attempts to make tablets were repeated. Tableting was carried out by placing the powders by hand into a tablet die in a manual bench top press. When compression pressure was applied, quantifiable amounts of capric acid were stuck on the tablet die due to it melting. This can be easily seen in **Figure 2**. Again, no photograph is included after compression of sodium caprate, as no residual material is on the tablet die and the appearance is the same as that of an unused clean die.

8. Labrasol, a liquid at room temperature, was added to each of the powder blends in **Table 1** at a ratio of 5/1 of fatty acid/Labrasol. Appropriate weights of the four powder blends were placed by hand in a tablet die, and formation of tablets attempted. A sizable portion of Labrasol squirted out of the die during the compression stage. **Figure 3** shows material on the outside of the die cavity after compression was attempted. It was not possible to make tablets with the Labrasol containing blends. No testing could be carried out on such tablets because of this problem. No further work was attempted using Labrasol incorporated into tablets due to the lack of success in this experiment.

C. Tablet Disintegration

9. The capric acid and sodium caprate tablets made in (B) were evaluated for disintegration behavior at 25°C and 37°C according to the official technique published in the United States Pharmacopeia. **Table 2** contains the results of this evaluation.

Table 2. Disintegration Time (minutes)

Tablet	25°C	37°C
Sodium Caprate	14 min 40 sec	12 min 10 sec
Sodium Caprate/Sorbitol	16 min 57 sec	10 min 40 sec
Capric Acid	Does not disintegrate within 2 hours	2 min 16 sec[1]
Capric Acid/Sorbitol	Does not disintegrate within 2 hours	2 min 11 sec[1]

[1]Tablet melts, and a layer of oil is observed on top of the bath water

D. Capsule Preparation and Dissolution

10. Capsules were prepared containing 28 mg of insulin in combination with 175 mg of medium chain fatty acids and medium chain fatty acid salts with and without 175 mg of Labrasol according to Watts *et al.* (WO 97/059030), cited in the Action. Dissolution was carried out on these capsules using USP apparatus II at 50 rpm with USP 6.8 Phosphate buffer and 100 mL of dissolution fluid. This volume of dissolution fluid was used to mimic the largest volume generally available to enteric coated dosage forms for dissolution *in vivo*. The rate of appearance of the fatty acid and insulin was monitored in the dissolution medium. The results are shown in **Table 3** below.

Table 3. Dissolution of Capsules

System	Analyte		% Dissolution[1,2]	
		15 min	**30 min**	**45 min**
C8 Acid [175 mg], Insulin [28 mg]	C8 Acid	45.6	55.3	67.2
	Insulin	6.9	8.8	15.1
C8 Acid [175 mg], Insulin [28 mg], Labrasol [175 mg]	C8 Acid	80.0	107.8	112.1
	Insulin	29.9	40.7	52.7
C8 Salt [175 mg], Insulin [28 mg]	C8 Salt	51.1	99.8	102.5
	Insulin	48.1	105.8	109.5
C8 salt [175 mg], Insulin [28 mg], Labrasol [175 mg]	C8 Salt	93.2	113.2	115.4
	Insulin	39.1	81.1	104.2
C10 Acid [175 mg], Insulin [28 mg]	C10 Acid	62.3	87.5	94.4
	Insulin	19.3	21.9	23.3
C10 Acid [175 mg], Insulin [28 mg], Labrasol [175 mg]	C10 Acid	48.5	89.2	100.9
	Insulin	11.3	45.6	68.4
C10 Salt [175 mg], Insulin [28 mg]	C10 Salt	0.8	102.6	107.3
	Insulin	0.0	109.9	116.5
C10 salt [175 mg], Insulin [28 mg], Labrasol [175 mg]	C10 Salt	39.8	109.3	112.4
	Insulin	0.0	51.8	81.6
C12 Acid [175 mg], Insulin [28 mg]	C12 Acid	NA	42.6	54.8
	Insulin	NA	74.9	80.9
C12 Acid [175 mg], Insulin [28 mg], Labrasol [175 mg]	C12 Acid	NA	75.6	91.8
	Insulin	NA	29.1	72.9
C12 Salt [175 mg], Insulin [28 mg]	C12 Salt	NA	100.3	101.9
	Insulin	NA	94.1	102.4
C12 Salt [175 mg], Insulin [28 mg], Labrasol [175 mg]	C12 Salt	NA	99.8	101.7

System	Analyte		% Dissolution[1,2]	
	Insulin	NA	21.8	24.5
C14 Acid [175 mg], Insulin [28 mg]	C14 Acid	NA	0.0	0.0
	Insulin	NA	68.1	110.7
C14 Acid [175 mg], Insulin [28 mg], Labrasol [175 mg]	C14 Acid	NA	17.7	19.5
	Insulin	NA	40.4	58.0
C14 Salt [175 mg], Insulin [28 mg]	C14 Salt	NA	0.0	0.0
	Insulin	NA	81.4	85.8
C14 Salt [175 mg], Insulin [28 mg], Labrasol [175 mg]	C14 Salt	NA	40.3	47.8
	Insulin	NA	75.2	91.3

[1] Corrected for sample volume removed for analysis
[2] Average of two capsules
NA Not Available

11. Results will be discussed in the order in which they appear in **Table 3**. The results for the caprylic acid capsules are shown first. Even though caprylic acid is a liquid at room temperature, only about two-thirds of the amount of caprylic acid in the caprylic acid capsule appears in the dissolution medium at 45 minutes. This is due to the fact that caprylic acid floats on the surface, and never disperses in the dissolution medium. The presence of Labrasol facilitates the dissolution of the caprylic acid, and all of the caprylic acid appears in the dissolution fluid from the caprylic acid/Labrasol capsules. Without Labrasol present, very little insulin goes into solution from the caprylic acid capsules, about 15 percent. The addition of Labrasol in the capsules substantially changes the insulin dissolution with about 50 percent of the insulin content being dissolved.

12. Contrary to the data for caprylic acid capsules, all the insulin and the sodium caprylate are fully dissolved in the dissolution media from the sodium caprylate capsules. All of the insulin and all of the sodium caprylate are also dissolved from the sodium caprylate/Labrasol capsules as well.

13. Similarly, the presence of the Labrasol made a substantial improvement in the dissolution of insulin from the capric acid capsules, with about 23 percent of the insulin being dissolved from the capric acid capsules versus about 68 percent from the capric acid/Labrasol capsules. There was little effect of the presence of Labrasol with the dissolution data for the capric acid. This was an unexpected result, as the data collected on disintegration analysis above indicate that capric acid floats on water, and does not disperse. Therefore, one would expect to see similarly poor dissolution for capric acid that was seen for caprylic acid. However, the density of capric acid at 37°C is similar to that of water, and the agitation of the paddle at 50 rpm appears to be sufficient to maintain dispersal. However, this dispersed capric acid was not able to impact the dissolution of the insulin; only the presence of Labrasol was capable of doing this. Therefore, these data indicate that little or no effect of capric acid is expected to be seen on the absorption of insulin in the absence of Labrasol. These data are consistent with the *Watts* patent.

14. All of the sodium caprate went into solution from both the sodium caprate capsules and the sodium caprate/Labrasol capsules. All of the insulin went into solution with the sodium caprate capsules. The presence of the Labrasol in the sodium caprate capsules appears to have depressed the dissolution of the insulin. This is the opposite effect of the Labrasol in the capsules containing capric acid.

15. In the case of sodium caprate, there are also differences in the dissolution of the insulin in the presence and absence of Labrasol. However, the effect here is opposite from that observed with the capric acid dissolution. Labrasol depresses the dissolution of the insulin from the sodium caprate/Labrasol capsules. These data indicate that the absorption enhancing effects of sodium caprate could be obviated, at least in part, by the presence of Labrasol. These data could not have been predicted from the disclosure of *Watts*.

16. There is a substantial difference between the dissolution of the lauric acid from the lauric acid capsules and the lauric acid/Labrasol capsules. About 55 percent of the lauric acid is dissolved from the lauric acid capsules as opposed to 92 percent from the lauric acid/Labrasol capsules. The rate of dissolution of the insulin was depressed in the capsules containing Labrasol. In neither case was the dissolution of the insulin complete, with about 81 percent and 73 percent dissolved from the lauric acid capsules and the lauric acid/Labrasol capsules, respectively.

17. All of the sodium laurate was released from the capsules for both the sodium laurate capsules as well as the sodium laurate/Labrasol capsules. All the insulin was dissolved from the sodium laurate capsules. However, as was seen with the sodium caprate/Labrasol capsules, the addition of Labrasol to the capsules suppresses the dissolution of the insulin. As drug must be dissolved to be absorbed, it appears that Labrasol in conjunction with sodium laurate will inhibit absorption of insulin.

18. No myristic acid was dissolved at all from the myristic acid capsules. About 20 percent was dissolved from the myristic acid/Labrasol capsules. The dissolution of the insulin was complete from the myristic acid capsules. Looking at these data versus the lauric acid capsule data, having no myristic acid going into solution improves insulin dissolution to the value one would expect in the dissolution medium alone. The insulin dissolution was substantially depressed by the presence of Labrasol here, as was seen with lauric acid. However, the extent of the suppression was greater.

19. The amount of sodium myristate dissolved from the sodium myristate capsules was below the limit of detection of the assay. This was not unexpected as it is well known that the solubility of sodium myristate is decreased substantially in the presence of inorganic salts (*J.Coll. Inter. Sci.* 291 (2005) pp543-549). Phosphate buffer was used in these experiments. Addition of Labrasol resulted in almost half of the sodium myristate being dissolved. This was a two-fold increase in the dissolution of sodium myristate with Labrasol relative to myristic acid with Labrasol. Unlike the data with myristic acid and Labrasol, no depression of insulin dissolution was seen with sodium myristate and Labrasol, with most of the insulin being dissolved by 45 minutes in both cases.

E. Animal Studies

19. Capsules were prepared containing 10 mg of alendronate, 10 mg of alendronate combined with 175 mg of capric acid, and 10 mg of alendronate combined with 175 mg of sodium caprate. These capsules were enteric coated and orally administered to dogs. Five dogs were used, and administration of each treatment was separated by 7 days. The dogs were housed in metabolism cages after the administration, and urine output was collected for 24 hours. The cages were rinsed at the end of the experiment and the rinse samples were also assayed to insure that alendronate excreted was assayed. Urine was assayed using a validated method for alendronate content. This methodology carried out in dogs is representative of the current standard method for determining alendronate absorption in humans for the approval of generic drugs. The amount absorbed directly relates to the amount absorbed from each of the capsules.

20. The average amount of drug excreted from the 5 dogs after each of the treatments is shown in Table 5 along with results of the statistical analysis. The data demonstrate that there was less absorbed from the alendronate/capric acid capsules than from the alendronate capsules. There was twice as much absorbed from the alendronate/sodium caprate capsules than from the alendronate capsules. The data were analyzed statistically by an analysis of variance. There were no statistically significant difference between the unenhanced alendronate capsules and the capric acid capsules. There was a significant difference between the sodium caprate capsules and both of the other treatments, as shown in **Table 4**.

Table 4. Average amount of drug excreted and statistical analysis – dog study

Treatment	Average Absorbed (mcg)	Ratio to unenhanced	P Value versus unenhanced	P value of Trt 2 to Trt 3
Unenhanced	24.4	1		
Capric acid	23.1	0.946	0.9002	0.0352
Sodium Caprate	48.7	2.00	0.0431	

F. Conclusions

21. In summary, there are a variety of ways in which significant differences can be demonstrated between medium chain fatty acid enhanced solid dosage forms and medium chain fatty acid salt enhanced solid dosage forms. These differences are seen in processing aspects necessary to make tablets and capsules, disintegration properties of tablets, and dissolution characteristics of capsules. Addition of Labrasol has impact on all the dissolution parameters for medium chain fatty acid capsules, but makes processing even more impossible. Addition of Labrasol can have a negative impact on parameters for medium chain fatty acid salt capsules. Co-administration of capric acid with alendronate may actually decrease absorption, and clearly does not improve it. Co-administration of sodium caprate with alendronate substantially improves absorption of alendronate.

22. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

TW Leonard
Thomas W. Leonard, Ph.D.

4 Mar 09
Date

FIG. 1

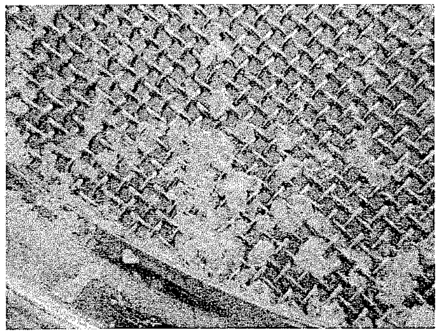

FIG. 2

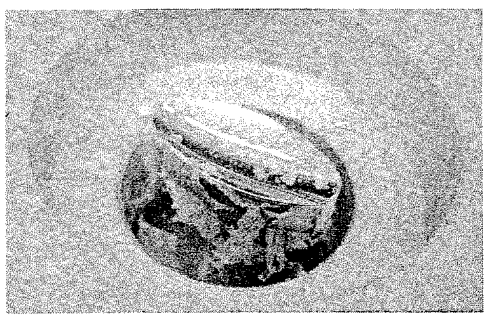

FIG. 3

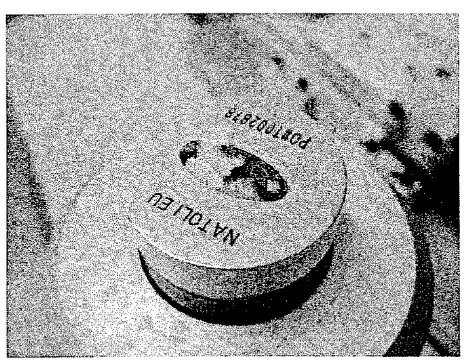

Exhibit A

THOMAS W. LEONARD
CURRICULUM VITAE

PERSONAL INFORMATION

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EDUCATIONAL BACKGROUND

Ph.D.	Pharmaceutics Medical College of Virginia Virginia Commonwealth University Richmond, VA	9/82
B.S.	Pharmacy College of Pharmacy University of South Carolina Columbia, SC	12/74
	Pre-Pharmacy Clemson University Clemson, SC	70-72

PROFESSIONAL EXPERIENCE

2004-present **Merrion Pharmaceuticals, LLC, Wilmington, NC**
Vice President & Chief Scientific Officer

Merrion is a specialty pharmaceutical oncology and drug delivery company, formed in 2004. At the time of formation, Merrion acquired laboratories, pilot manufacturing facilities, and intellectual property (25 issued and in process patents) focused on enhanced and sustained oral drug delivery, and membrane permeation enhancer technology (vaccine and blood-brain barrier oriented). Merrion has 3 programs in the clinic, one of which is in Phase II in prostate cancer. I manage clinical research, US regulatory affairs, manage and develop the patent portfolio, and provide scientific leadership for day to day operations as well as corporate strategy, business development, and corporate fundraising.

<u>1999 – 2004</u> **Endeavor Pharmaceuticals, Inc., Wilmington, NC**
Vice President & Chief Scientific Officer

I served as the Chief Scientific Officer for Endeavor Pharmaceuticals, an emerging specialty pharmaceutical company. After gaining FDA approvable status for our lead product and patent coverage for our portfolio of hormone therapy products, we sold all the assets of Endeavor to Barr Laboratories.

Endeavor was originally created as a joint venture between aaiPharma and Schering AG (Berlex Laboratories). As part of a management team established in 1999, we created a new business plan, and I developed a comprehensive intellectual property strategy. The CEO and I raised $46M in additional capital. Commensurate with raising additional capital, I created a Medical Advisory Board consisting of world-recognized experts. Subsequent to funding, I staffed a research and development department oriented towards an outsourcing model, opened 4 INDs for three products, and filed and gained approvable status for an NDA on our lead product. I served as head of the Medical Affairs Division, and represented the company to potential investors, key opinion leaders and media, including the *Wall Street Journal* and *Forbes*. The intellectual property portfolio I developed has resulted in patent protection for all products under development.

<u>1994 – 1999</u> **aaiPharma, Inc., Wilmington, NC**

During my tenure, aaiPharma was the largest CMC-based contract research organization in the world. I had administrative, budget, revenue, and scientific responsibilities for areas under my supervision.

1997 – 1999 Senior Director, Product Development

I carried out a consolidation of the Formulation Division with the required analytical support into the Product Development Division. I was responsible for all formulation development, scale-up/transfer, and associated analytical development. I initiated a facility and staff expansion to increase analytical capabilities in my Division by 50%. I simultaneously served as Acting Director of the Manufacturing Division for 6 months of 1998 while recruiting and training a new Director. I headed the efforts to obtain NDA approval for a contract product, carried out five new product launches and opened a new manufacturing suite dedicated to solid dosage forms of highly potent compounds. I co-chaired a corporate development and validation team for automated report generator for all AAI analytical laboratories. My total staff, including the Manufacturing Division, was over 110 people.

1994 – 1997 Director, Formulations Development Division

I increased the external contract business in formulation development by an average of 20% per year during my 5 years at AAI. This was accomplished by improving quality, communication, and tightening up the contract bidding and administration procedures.

As part of the quality and communication improvements, I created a Product Transfer Group and implemented a procedure for internal and external transfer to manufacturing. I expanded the formulation processing room capacity by 50%, and implemented engineering designs and procedures to handle highly potent compounds. Work carried out during my tenure lead to approval of over 10 ANDAs, and 2 NDAs. We also completed CMC sections for over 10 INDs. The staff of over 25 professionals carried out all types of conventional formulation development.

<u>1982-1994</u> American Home Products

From 1982 until 1994 I worked in the Rouses Point, NY facility of American Home Products (now called Wyeth). During the first 6 years, this facility was part of Ayerst Laboratories. Wyeth and Ayerst were merged into one operating unit in late 1987/early 1988, and I spent the remainder of my career there in the merged company.

1988 – 1994 Wyeth-Ayerst Research, Rouses Point, NY, Associate Director, Liquid Formulations and Parenteral Development Sections

I provided administrative and scientific leadership for two sections which were responsible for all non-solid dosage form development, including pre-clinical, clinical, and market product development of parenterals, oral liquids, topicals, transdermals, intranasals, vaginals, and rectals. In addition to these line management responsibilities, I also served as a corporate project team leader for an AIDS compound (licensed in and cancelled during Phase II/III trials), and for novel treatments for menopause. The HRT team launched a product in South America, filed for approval of a product in the EU, and initiated development of products in the USA during my tenure. I supervised multiple external research programs, and participated as scientific reviewer for external licensing candidate evaluations.

1982-1988 Ayerst Laboratories, Inc., Rouses Point, NY
1985-1988 Section Head, Biopharmacy and Experimental Formulations

I provided administrative and scientific leadership for a section of up to 12 scientists conducting pharmacokinetic and biopharmaceutical analyses, bioanalytical work, novel formulation development and computer-aided dosage form analyses and design.

1983-1985 Section Head, Transdermal and Topical Formulations
1982-1983 Group Leader, Biopharmacy

<u>1978 – 1982</u> Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, Graduate Teaching Assistant

<u>1978 – 1982</u> Hospital and Community Relief Pharmacist

<u>1975 – 1978</u> Crafts Drug Stores, Spartanburg, SC, Community Pharmacist, Assistant Store Manager

1975 **Anderson Memorial Hospital, Anderson, SC, Hospital Pharmacy Intern**

1974 **College of Pharmacy, University of South Carolina, Columbia, SC, Undergraduate Research and Teaching Assistant**

LICENSURE

South Carolina, 1975, examination
Virginia, 1978, reciprocation (inactive status)

PROFESSIONAL ORGANIZATIONS

American Association of Pharmaceutical Scientists (AAPS)
- Regional Meeting Planning Committee, 1997-1998.

Parenteral Drug Association
- Parenteral Drug Association Foundation
  - Awards and Grants Committee – Reviewer, 1989; Standing Committee Member, 1990-1998.

Sigma Xi
Champlain Valley Management Club
- Board member 1983-1990.

Controlled Release Society (CRS)
Drug Information Association (DIA)
North American Menopause Society (NAMS)

FELLOWSHIPS and AWARDS

- 1981 Henry S. Wellcome AFPE Pharmaceutics/Biopharmaceutics Fellow
- American Foundation for Pharmaceutical Education Fellow, 1980-1982
- Honorable Mention: 1979 National Science Foundation Graduate Fellowship Competition
- A.D. Williams Fellow, 1978-1979
- Rho Chi Honorary Pharmaceutical Fraternity
- Phi Kappa Phi Honor Society

PODIUM PRESENTATIONS

1. IBC Life Sciences TIDES Conference, Boston MA, May 1-5, 2005. Topic: "Oral Delivery Techniques for Poorly Permeable Compounds."

2. 10^{th} Anniversary Drug Delivery Technologies & Deal Making Summit, New Brunswick, NJ, sponsored by the Strategic Research Institute of New York, 26-28 September, 2005. Topic: "Gastrointestinal Permeation Enhancing Technology for Poorly Permeable Compounds."

3. The British Pharmaceutical Conference & Exhibition 2006 (BPC), Manchester, United Kingdom, September 4 - 6, 2006. Session title: Living in a material world: new materials in drug delivery. Presentation Title: "Advancing gastro-intestinal permeation enhancement formulations into the clinic."

3. Future of Male Contraception, Seattle, Washington, September 27-28, 2007. Topic: "Oral Acyline."

4. 13th Annual Drug Delivery Partnerships Conference, Las Vegas, NV, January 20-23, 2009. Presentation: "Merrion's GIPET® Delivery Technology."

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3. T.W. Leonard, B. J. Kline, and J.H. Wood. "HPLC Determination of Carboxytolbutamide in Human Urine." Abstracts AphA Academy of Pharmaceutical Sciences, 11(2): 128 (1981).

4. K.L. Garrettson, J.H. Wood, and T. W. Leonard. "Age Dependent Changes in Theophylline Elimination." In: Environmental Effects on Maturation, Edited by V. Hunt, M.K. Smith, and D. Worth. Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982).

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7. T.W. Leonard, J.H. Wood. "Pharmacokinetic Modeling of Bladder Resorption for Several Drugs." Ibid, 12(2): 169 (1982).

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9. J.H. Wood and T. W. Leonard. "Kinetic Implications of Drug Resorption from the Bladder." Drug Metabolism Review, 14(3): 407-423 (1983).

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12. L. Q. Semmens, T. W. Leonard, E. Ingersoll, J. Balchunis. "Identifying the Critical Elements of a Technology Transfer Operation." Pharmaceutical Technology, 21(11): 74-78 (1997).

13. T.W. Leonard, J. Swarbrick, R.R. Whittle, E.N. Hill, G.W. Ponder. "Characterization of Active Components in Conjugated Equine Estrogens." Menopause, 9(6): 481 (2002).

14. W.H. Utian, T.W. Leonard, A.D. Davis, R.Y. Vega. "The Safety and Efficacy of a New Synthetic 10-Component, Modified Release Conjugated Estrogens Tablet." Menopause, 9(6): 480 (2002).

15. W.H. Utian, T.W. Leonard, A.D. Davis, R.Y. Vega. "Efficacy and Safety of a New Synthetic 10-Component, Modified Release Conjugated Estrogens Tablet for Treatment of Vasomotor Symptoms in Postmenopausal Women." Fertility & Sterility, 78(3), Suppl. 1: 24 (2002).

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